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REMARKS

The Office action of June 18, 2004, has been carefully considered.

Claims 19 through 34 have been rejected under 35 USC 112, second paragraph, as being indefinite on a number of grounds.

In Claim 19, it is alleged that "said immunoglobulins" has no antecedent basis, and this term has now been changed to "said IgA."

Moreover, Claim 19 has been amended to recite that IgA is produced by the host, and it is this IgA that is removed and purified. Thus, the claim is directed to a method for production of IgA.

Claim 20 has been canceled, and those claims dependent on Claim 20 now depend from Claim 16.

The misspelling noted in Claim 21 has been corrected.

The term "cholesterol esters" has been removed from Claim 29, and is now found in new Claim 35 which depends from Claim 29.

Withdrawal of this rejection is accordingly requested.

In addition to the amendments discussed above, Claim 16 has been amended to clarify the subject matter of the invention, and new sets of claims corresponding to originally filed claims have been added depending from independent claims 18 and 19.

Claims 16 and 17 have been rejected under 35 USC 102(b) as anticipated by de Haan et al.

De Haan et al discloses intra-nasal administration of a liposomal formulation containing influenza antibodies. As is evident from page 156 of this reference, the liposomes used are conventional liposomes which differ structurally from the vesicles according to the claimed invention.. The structure of such vesicles is discussed on page 5, lines 19 through 36 of

the present specification, and a number of points of distinction are given. These vesicles are disclosed for example in the Roux et al patent, U.S. Patent No. 5,908,697, which has been cited in the present Office action, as well as in the references given on page 5 of the specification. The administration of antibodies in such vesicles is also disclosed in WO 99/16468, corresponding to co-pending U.S. patent application 09/536,153.

Further evidence regarding the structural differences between the vesicles of the invention and conventional liposomes was provided during the prosecution of U.S. application 09/536,153, and will be provided to the Examiner upon request. However, it can be stated that conventional liposomes are not made of a regular stack of concentric bilayers of amphiphilic compounds alternating with layers of water or aqueous solution or a solution of polar liquid.

Based upon the differences between the vesicles of the invention and conventional liposomes, withdrawal of this rejection is requested.

Claims 20 through 27, 31 and 34 have been rejected under 35 USC 103(a) over de Haan et al, by itself or in combination with Doerschuk et al.

As all claims in this group are based upon Claim 20, which has been canceled, Applicants submit that the rejection has been rendered moot, and withdrawal of this rejection is requested.

Claims 16 through 34 have been rejected under 35 USC 103(a) over de Haan et al by itself or in combination with Doerschuk, and further in combination with Roux et al.

The Doerschuk reference has apparently been cited only to teach that it is well known to purify immunoglobulins, but is not otherwise relevant to the subject matter of the invention.

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The Roux et al patent has been cited to show the vesicles of the invention. While such vesicles were known at the time of filing this application, and were in fact known for administration of antibodies (as discussed above), it was not known that mucosal administration of antibodies utilizing the vesicles of the invention would be effective for inducing a systemic response.

De Haan et al disclose the use of liposomes as a mucosal immunoadjuvant. As is noted in the abstract and on page 159, first paragraph, a negatively charged phospholipid must be used with the liposomes; beneficial results are not obtained utilizing a neutral or zwitterionic phospholipid. An attempt to explain the necessity of using a negatively charged phospholipid is given on page 161.

To the contrary, the claimed invention does not require a negatively charged phospholipid, and in the examples of the present application, zwitterionic phospholipid, phosphatidylcholine, was used. According to de Haan et al, this phospholipid gives negative results in their experiment (page 159, column 2).

Thus, it is surprising in view of de Haan et al that it is possible to induce a strong immune response utilizing phospholipids which are not negatively charged and this is clear evidence that the mechanism of action of the invention is different from that of de Haan et al.

Moreover, it is specified in de Haan et al that the vaccination protocol should enable reaching the totality of the pulmonary tract, including the pulmonary alveolus (page 156, last paragraph). In the discussion on page 161, de Haan et al explain that the role of alveolar macrophages is of primary importance. The other hypothesis in the discussion to account for the result is also based on the role of the lungs

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rather than on the role of the mucosa of the nostrils.

To the contrary, the protocol used in the examples of the present application, in which a small volume of material was deposited into each nostril, is intended to avoid any introduction of the antigen further than the nostril. This is further clear evidence that the mechanism of action of the claimed invention is different from that of de Haan et al.

In the experiments of de Haan et al, administration of empty liposomes two days before the antigen produces results as good as, or even better than, the protocol in which the liposomes and antigen are administered together. The authors describe a mechanism in which the lipids from the liposomes inhibit the alveolar macrophages, and this allows the antigen injected after this inhibition to avoid any destruction by the macrophages, and therefore to elicit a specific immune response.

The fact that these results are substantially the same strongly indicates that the antigens must be liberated from the liposomes before reaching before reaching the lungs, in order to avoid capture by the alveolar macrophages at the same time as the liposomes. The consequence of this teaching is that one of ordinary skill in the art should not use a more stable vesicle (such as one according to the claimed invention), in place of a less stable liposome as used according to de Haan et al.

Those of ordinary skill in the art understand that a vesicle having a liquid crystal structure which is ordered is necessarily more stable that a liposome which does not have such a structure, and would not utilize the more stable liquid crystal vesicle for administration of antigens.

Thus, even with the knowledge of WO 99/16468 and the Roux et al patent, one of ordinary skill in the art would not be

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inclined to utilize the vesicles described in those references as antigen carriers for antigens as discussed in de Haan et al, for mucosal administration. One of ordinary skill in the art would understand that should those vesicles reach the lungs, the antigen which has been retained by the stable vesicles would be destroyed by the alveolar macrophages. In view of this teaching of de Haan et al, one of ordinary skill in the art would have predicated a negative result with little or no induction of an immune response utilizing the vesicles of the invention. This is clearly contrary to the result obtained and described in the present application.

Withdrawal of this rejection is accordingly requested.

Claims 16 through 34 have been rejected under 35 USC 103(a) over Wassef et al in combination with de Haan et al by itself or in combination with Doerschuk et al and Roux et al.

The de Haan et al, Doerschuk et al and Roux et al references have been discussed in detail above.

The Office action alleges that Wassef et al teach the successful use of multilamellar vesicles as carriers for vaccines.

The carriers for vaccines taught by Wassef et al are liposomes, which are conventional liposomes and not the multilamellar vesicles of the claimed invention. The Office action admits that Wassef et al does not teach the mucosal route of administration. Moreover, Wassef et al teaches the use of phosphatidylcholine for the liposomes, which cannot be used according to de Haan et al. Accordingly, one of ordinary skill in the art would not find Wassef et al to be useful for combination with de Haan et al and withdrawal of this rejection is requested.

In view of the foregoing amendments and remarks, Applicants submit that the present application is now in

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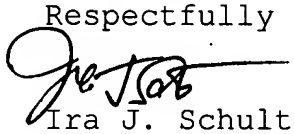
condition for allowance. An early allowance of the application with amended claims is earnestly solicited.

Respectfully submitted,



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